

The opinion in support of the decision being entered today
is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte BOJIDAR M. STANKOV

Appeal 2007-3261
Application 09/854,802
Technology Center 1600

Decided: September 20, 2007

Before DEMETRA J. MILLS, LORA M. GREEN, and RICHARD M.
LEBOVITZ, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the final rejection of claims 16-18
and 20-24. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF CASE

Melatonin (N-acetyl-5-methoxytryptamine) is a naturally-occurring
compound which is known to induce and improve the depth and quality of
sleep (Spec. 2). Because of its short half-life in the blood, exogenously
administered melatonin has been found to be insufficient to regulate sleep
(Spec. 2-3). To address this problem, melatonin has been administered in

retardant formulations to increase its effectiveness (Spec. 3). The “subject of this invention” are “new formulations for the controlled release of melatonin able to ‘mimic’ the physiological melatonin pattern in the peripheral blood” (Spec. 3). The pending claims are directed to a controlled release melatonin tablet comprising a slow release nucleus and a fast release cortex coating on the nucleus. Both the nucleus and cortex comprise melatonin.

There are three rejections on review in this proceeding:

1) Claims 16-18 and 20-24 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description (Answer 5);

2) Claims 16-18 and 20-24 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement for the full scope of the claims (Answer 4); and

3) Claims 16-18 and 20-24 stand rejected under 35 U.S.C. § 112, second paragraph, as being incomplete (Answer 6).

Within each rejection, the claims stand or fall together because separate reasons for the patentability of any individual claim were not provided. *See* 37 C.F.R. § 41.37(c)(1)(vii). We select claim 16, the only independent claim on appeal, as representative of all the claims to decide the issues in this proceeding. Claim 16 reads as follows:

A controlled release melatonin tablet which comprises:

(a) a slow release nucleus comprising melatonin, hydroxypropyl methylcellulose, a lubricant, a volume excipient and a glidant, wherein 95% of the melatonin is released within 5 hours in an oscillating tray containing gastric/intestinal juice at 37°C;

(b) a fast release cortex coating on said nucleus which comprises melatonin, hydroxypropyl methylcellulose, a lubricant, a volume excipient and a glidant, wherein at least

95% of the melatonin is released within 10 minutes in an oscillating tray containing gastric/intestinal juice at 37°C.

DISCUSSION

Enablement rejection

The Specification provides one working example of a controlled release melatonin tablet comprising a slow release nucleus and a fast release cortex as recited in claim 16 (Spec. 7-8). The Examiner contends that the Specification is only enabled for this single embodiment, but does not enable other formulations (Answer 4). Thus, the Examiner concludes that the Specification is not in compliance with the enablement requirement of § 112, first paragraph, because it does not enable persons of skill in the art to make and use the full scope of the claims (Answer 4).

“To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). In *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), a number of factors were set forth which may be considered in determining whether a disclosure would require undue experimentation. These factors are as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Wands*, 858 F.2d at 737,

8 USPQ2d at 1404. Not all the factors need not be reviewed when determining whether a disclosure is enabling. *See Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the Wands factors “are illustrative, not mandatory. What is relevant depends on the facts.”); *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1135 (Fed. Cir. 1999).

In order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *Wright*, 999 F.2d at 1562, 27 USPQ2d at 1513. The Examiner made the following key findings with respect to the factors set out in *Wands*:

The state of the prior art and the predictability or lack thereof in the art. “[T]he prior art indicates that HPMC [hydroxypropyl methylcellulose] is a known retardant and dose of drug and amount and type of excipients all have an effect on release rates (See Bromet et al. (US Pat. 5,879,710), Column 5, lines 1-5; Lee et al. (1999), pages 74-77). The Appellant argues that the prior art does not exhibit the release profile of the claimed invention as represented by Figure 1, yet the claimed invention also contains HPMC, a known retardant. As such, it appears that predictability in the art is low” (Answer 4-5).

The amount of direction or guidance present and the presence or absence of working examples. “The Specification appears to provide only one formulation that exhibits the release profile that the Appellant argues is the exhibited by the claimed invention” (Answer 5).

The breadth of the claims and the quantity of experimentation needed. “The claims are broad in that the only mentioned components are HPMC,

melatonin, lubricant, volume excipient and glidant. As such, . . . undue experimentation [would be required] in order to make and/or use the invention commensurate in scope with the claims, i.e. determining what combination of HPMC, melatonin, lubricants, volume excipients and glidants would result in the release profile claimed” (Answer 5).

In our opinion, the Examiner has set forth a reasonable basis to doubt the enablement provided for claim 16. In particular, the Examiner cites the Bromet patent (US 5,879,710, issued Mar. 9, 1999) as evidence of unpredictability. Bromet describes a melatonin tablet comprising sustained- and rapid-release layers (Bromet, at cols. 5-6). The sustained-release layer (A) is for slow release of the melatonin (Bromet, at col. 3, ll. 60-65) and comprises HPMC (col. 5, ll. 1-5 and 63 (“methocel”)) like the corresponding slow release nucleus of the claimed invention (Spec. 4: 8-10). At column 5, lines 1-5, referred to in the Answer, among the list of ingredients in the sustained-release layer (beginning at col. 4, l. 50), Bromet describes HPMC (“methocel”) as a retardant present “at a weight concentration of 3% to 20%, and preferably 5 to 15%.” Thus, Bromet’s disclosure would have led persons of skill in the art to reasonably expect that 3% to 20% HPMC in a tablet would result in the sustained release of melatonin.

Bromet’s rapid-release layer, however, does *not* contain HPMC in contrast to the fast release cortex of the claimed invention, which serves the same function to release melatonin rapidly upon administration (Bromet, at col. 3, l. 66 to col. 4, l. 2; Spec. 4: 1-4 and 10-12). Instead, it contains disintegrant to enhance release (Bromet, at col. 5, ll. 38-44).

In the only example provided in the instant Specification, the fast release cortex layer contains 8.8% HPMC (Spec. 8: 19) – which falls within

the range of “3% to 20%” described by Bromet to achieve the *slow-release* of melatonin. However, according to the Specification, when present in the fast release cortex, it releases substantially all the melatonin within 10 minutes (Spec. 11). This is opposite to what would have been expected from Bromet’s teaching: It would have been predicted that the addition of HPMC to the cortex would lead to slow release, rather than fast release as shown in the Specification. Thus, we agree with the Examiner that the formulation art with respect to the release of melatonin was unpredictable.

Furthermore, as noted by the Examiner, the Specification provides no guidance on what amounts of HPMC, lubricant, volume excipient, and glidant to use in order to achieve the claimed release profiles for the slow release nucleus and the fast release cortex (Answer 5). Particularly with respect to the fast release cortex, the claim requires “melatonin, [HPMC], a lubricant, a volume excipient and a glidant,” but the Specification does not specifically identify these components in the fast release cortex, let alone provide guidance on what amounts to use to achieve the recited release of “within 10 minutes in an oscillating tray containing gastric/intestinal juice at 37°C.” This deficiency independently provides sufficient reason to question the enablement for the entire scope of claim 16.

When, as here, the Examiner has set forth adequate doubt as to the enablement of the claim, the burden shifts to the patent applicant to provide rebuttal arguments or evidence. Appellant argues that it would only require

“a minimum amount of experimentation . . . to make useful compositions within the scope of the claims” (Sub. App. Br. 5¹). Appellant also argues:

These claims are specific to a particular material [melatonin] and from this perspective are quite narrow. The recitation of the other ingredients is made in terms that are specific of to materials or classes of materials that are well known and are exemplified in the specification. The art of making controlled release formulations for oral administration to humans has generated many thousands of patents in recent years and there are many textbooks and courses that have been devoted to this subject. Since the present claims deal with only one substance, this variable is not present in the appealed claims.

(Sub. App. Br. 6.)

We do not find Appellant’s argument sufficient to rebut the rejection for lack of enablement. We acknowledge that controlled release formations were known in the art prior to the application filing date. However, with respect to a controlled release tablet comprising melatonin – the same active pharmacological agent recited in claim 16 – Bromet’s teaching about the amounts of HPMC utilized in a slow- or sustained-released composition would have lead persons of skill in the art to reasonably doubt the scope of enablement for claim 16. Appellant has not responded to this issue nor explained how the Specification provides guidance on a fast release cortex comprising “melatonin, [HPMC], a lubricant, a volume excipient and a glidant” as recited in claim 16. Because the Examiner’s reasons for doubting the scope of enablement remain unrebutted, we affirm the rejection of claims 16-18 and 20-24 under § 112, first paragraph, for lack of enablement.

¹ This is a reference to the Substitute Appeal Brief, date stamped March 2, 2006.

Written description rejection

The Examiner contends that the claims do not comply with the written description requirement.

First, the Examiner asserts that since 95% of the melatonin was released “within the 5th hour” and not “within five hours” the Specification does not describe the limitation in claim 16 that “wherein 95% of the melatonin is released within 5 hours” (Answer 6). The same assertion is made for the limitation wherein 95% of the melatonin is released within 10 minutes.

Secondly, the Examiner asserts that

the Appellant has amended the claims to indicate that the fast release cortex also contains a lubricant, volume excipient and glidant. However, the Specification does not appear to indicate that the “cortex” contains lubricant or a glidant. The only example set forth contains, in addition to melatonin and HPMC, lactose, a bulking agent, i.e. volume, titanium dioxide, a pigment, and ethyl alcohol and water, solvents, which presumably are evaporated away in order to form the cortex (See Pg. 8, lines 15-23).

(Answer 6.)

We find that the Specification adequately describes the claim limitations “wherein 95% of the melatonin is released within 5 hours” and “wherein at least 95% of the melatonin is released within 10 minutes.” The Specification expressly describes the release of melatonin within the recited times (Spec. 4: 1-7; 5: 29-32; 12: 1-5). In addition, as argued by Appellants, “[t]he specification is addressed to one of ordinary skill in the art of controlled release pharmaceuticals and it is well known that all measurements of controlled released products are based on a cumulative

total of release active ingredient after a specified time” (Reply Br. 1²). As shown in Lee,³ provided by the Examiner, “a typical release curve . . . shows that the release vs. time is computed cumulatively and is not based on a release within any period of time within the middle of the test” (Reply Br. 2).

With respect to the second ground, however, we concur with the Examiner’s reasoning. The Examiner has the initial burden of presenting evidence or reasons why a person skilled in the art would not recognize in an applicant’s disclosure a description of the invention defined by the claims. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976). In this case, the Examiner finds that the Specification describes “volume excipients, gliding and lubricating excipients” (Spec. 7: 1-2) for the slow release layer. However, the Examiner states the Specification does not teach the use of these additives to obtain the rapid release profile required for the rapid release cortex. (Answer 6). While there is no requirement that the invention be claimed in the identical wording that was used in the specification, there must be sufficient disclosure to show one of skill in this art that the inventor “invented what is claimed.” See *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 1000, 54 USPQ2d 1227, 1235 (Fed. Cir. 2000). In view of the lack of literal support for the limitation, it is our opinion that the Examiner has reason to question the written description for the recited limitation, shifting the burden to Appellant to rebut it. Because Appellant does not address this deficiency in either the Substitute Appeal Brief or

² This is a reference to the Reply Brief dated Feb. 5, 2007.

³ Lee, *Int. J. Pharmacol.*, 188: 71-80 (1990).

Reply Brief, we affirm the rejection of claims 16-18 and 20-24 for lack of written description.

Indefiniteness rejection

Claims 16-18 and 20-24 stand

rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: (2) granulation, (4) addition of the retardant excipients, lubricants, volume and gliding excipients and (7) application of the melatonin solution under pressure on the tablets for the formation of the “cortex”. Specification discloses that stages (2), (4) and (7) are essential for the preparation of the formulations which are the subject of the invention (Pg. 8, lines 27, 28).

(Answer 6.)

We reverse this rejection. A specification must conclude with claims “particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.” 35 U.S.C. § 112, ¶ 2 (2000). The purpose of § 112, ¶ 2, is to “reasonably apprise those skilled in the art of the scope of the invention.” *Miles Labs., Inc. v. Shandon, Inc.*, 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993). It is the purpose of the written description, not the claims, to describe how to make and use the invention. 35 U.S.C. § 112, ¶ 1 (2000). In this case, the claims are directed to a composition of matter. It is not necessary under § 112, ¶ 2 to recite the steps for making the composition in the claim; that function is the purpose of the written description.

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TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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